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Fig. 1

ATGTCCATGA	ACTGCTGAGT	GGATAAACAG	CACGGGATAT	CTCTGTCTAA	- 96
AGGAATATTA	CTACACCAGG	AAAAGGACAC	ATTTCGACAAC	AGGAAAGGAG	- 46
CCTGTACACAG	AAAACCACAG	TGTCCTGTGC	ATGTGACATT	TCGCC	- 1
ATG GGA AAC AAC TGT TAC AAC GTG GTG GTC ATT GTG CTG CTG CTA	45				
Met Gly Asn Asn Cys Tyr Asn Val Val Val Ile Val Leu Leu Leu					
GTG GGC TGT GAG AAG GTG GGA GCC GTG CAG AAC TCC TGT GAT AAC	90				
Val Gly Cys Glu Lys Val Gly Ala Val Gln Asn Ser Cys Asp Asn					
TGT CAG CCT GGT ACT TTC TGC AGA AAA TAC AAT CCA GTC TGC AAG	135				
Cys Gln Pro Gly Thr Phe Cys Arg Lys Tyr Asn Pro Val Cys Lys					
● H4-1BB FI ●					
AGC TGC CCT CCA AGT ACC TTC TCC AGC ATA GGT GGA CAG CCG AAC	180				
Ser Cys Pro Pro Ser Thr Phe Ser Ser Ile Gly Glu Pro Asn					
● H4-1BB FII ●					
TGT AAC ATC TGC AGA GTG TGT GCA GGC TAT TTC AGG TTC AAG AAG	225				
Cys Asn Ile Cys Arg Val Cys Ala Gly Tyr Phe Arg Phe Lys Lys					
TTT TGC TCC TCT ACC CAC AAC GCG GAG TGT GAG TGC ATT GAA GGA	270				
Phe Cys Ser Ser Thr His Asn Ala Glu Cys Glu Cys Ile Glu Gly					
TTC CAT TGC TTG GGG CCA CAG TGC ACC AGA TGT GAA AAG GAC TGC	315				
Phe His Cys Leu Gly Pro Gln Cys Thr Arg Cys Glu Lys Asp Cys					
AGG CCT GGC CAG GAG CTA ACG AAG CAG GGT TGC AAA ACC TGT AGC	360				
Arg Pro Gly Gln Glu Leu Thr Lys Gln Gly Cys Lys Thr Cys Ser					
● H4-1BB RII ●					
TTG GGA ACA TTT AAT GAC CAG AAC GGT ACT GGC GTC TGT CGA CCC	405				
Leu Gly Thr Phe Asn Asp Gln Asn Gly Thr Gly Val Cys Arg Pro					
● H4-1BB RII ●					
TGG ACG AAC TGC TCT CTA GAC GGA AGG TCT GTG CTT AAG ACC GGG	450				
Trp Thr Asn Cys Ser Leu Asp Gly Arg Ser Val Leu Lys Thr Gly					
ACC ACG GAG AAG GAC GTG GTG TGT GGA CCC CCT GTG GTG AGC TTC	495				
Thr Thr Glu Lys Asp Val Val Cys Gly Pro Pro Val Val Ser Phe					
TCT CCC AGT ACC ACC ATT TCT GTG ACT CCA GAG GGA GGA CCA GGA	540				
Ser Pro Ser Thr Thr Ile Ser Val Thr Pro Glu Gly Gly Pro Gly					
GGG CAC TCC TTG CAG GTC CTT ACC TTG TTC CTG GCG CTG ACA TCG	585				
Gly His Ser Leu Gln Val Leu Thr Leu Phe Leu Ala Leu Thr Ser					
GCT TTG CTG CTG GCC CTG ATC TTC ATT ACT CTC CTG TTC TCT GTG	630				
Ala Leu Leu Leu Ala Leu Ile Phe Ile Thr Leu Leu Phe Ser Val					
CTC AAA TGG ATC AGG AAA AAA TTC CCC CAC ATA TTC AAG CAA CCA	675				
Leu Lys Trp Ile Arg Lys Lys Phe Pro His Ile Phe Lys Gln Pro					
TTT AAG AAG ACC ACT GGA GCA GCT CAA GAG GAA GAT GCT TGT AGC	720				
Phe Lys Lys Thr Thr Gly Ala Ala Gln Glu Glu Asp Ala Cys Ser					

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Fig.1 cont'd

TGC CGA TGT CCA CAG GAA GAA GAA GGA GGA GGA GGA GGC TAT GAG 785
 Cys Arg Cys Pro Glu Glu Glu Glu Glu Glu Glu Glu Tyr Glu

CTG TGA
 Leu ---

771

TGTA	CTATCC	TAGG	GATGT	GTGGG	CCGAA	ACCG	GAGA	AGC	ACT	AGG	ACCC	821
CACCA	TCCTG	TGGA	ACAGCA	CAAG	CAACCC	CACCA	CCCC	CTG	TTCT	TAC	ACA	871
TCAT	CCTAG	TGAT	GTGTGG	GCGC	GCACCT	CATCC	AAGTC	TCTT	CTA	AACG		921
CTAAC	CATATT	TGTCT	TTTACC	TTTT	TTTAAAT	CTTTT	TTTAA	ATTT	AAATTT			971
TATGT	GTGTG	AGTGT	TTTGC	CTGC	CCTGTAT	GCAC	ACGTGT	GTGT	GTGTGT			1021
GTGTG	TGACA	CTCCT	GATGC	CTGAG	GAGGT	CAGAA	GACAA	AGGG	TTGGTT			1071
CCATA	AAGAAC	TGGAG	TTATG	GATGG	CTGTG	AGCC	GGNNG	ATAGG	TCGGG			1121
ACGG	GACCT	GTCTT	CTTAT	TTTA	ACGTGA	CTGT	ATA	AAAA	AAAAAT			1171
GATATT	TCGG	GAATT	GTAGA	GATT	GTCTG	ACACC	TTCT	AGTT	AATGAT			1221
CTAAG	AGGAA	TTGTT	GATAC	GTAG	TATACT	GTAT	ATGTGT	ATGT	ATATATGT			1271
ATATG	TATAT	ATAAG	ACTCT	TTTAC	TGTCA	AAGT	CAACCT	AGAG	TGTCTG			1321
GTTAC	CAGGT	CAATTT	TATT	GGAC	ATTTTA	CGTC	CACACAC	ACAC	CACACAC			1371
ACACA	CACAC	ACGTT	TATAC	TACGT	ACTGT	TATC	GGTATT	CTAC	GTCTATA			1421
TAATG	GGGATA	GGGT	AAAAGG	AAAC	CAAAAG	GTGAG	TGATA	TTAT	TGTGGA			1471
GGTG	ACAGAC	TACCC	CTTCT	GGGT	ACGTAG	GGAC	AGACCT	CCTT	CGGACT			1521
GTCTA	AAACT	CCCCT	TAGAA	GTCT	CGTCAA	GTTCC	CGGAC	GAAG	AGGACA			1571
GAGG	AGACAC	AGTCC	GAAAA	GTTAT	TTTTTC	CGGCA	AAATCC	TTTC	CCCTGTT			1621
TCGT	GACACT	CCACCC	CTTG	TGGAC	ACTTG	AGTGT	CATCC	TTGC	GCCGGA			1671
AGGT	CAGGTG	GTACCC	GTCT	GTAG	GGGCGG	GGAG	ACAGAG	CCGC	GGGGGA			1721
GCTAC	GAGAA	TCGAC	TACACA	GGGC	GCCCCG	GGCT	TCGCAA	ATGA	AACTTT			1771
TTTA	ATCTCA	CAAGT	TTTCGT	CCGG	GCTCGG	CGGAC	CTATG	GCGT	CGATCC			1821
TTATT	ACCTT	ATCCT	TGGCGC	CAAG	ATAAAA	CAACC	AAAAG	CCTT	GACTCC			1871
GGTAC	TAATT	CTCC	CTGCCG	GCCCC	CGTAA	GCATA	AACGCG	GCGA	TCTCCA			1921
CTTTA	AAGAAC	CTGG	CCGCGT	TCTG	CCCTGGT	CTCG	CTTTG	TAA	ACGGTTC			1971
TTACA	AAAAGT	AATT	AGTTCT	TGCT	TTTCAGC	CTCCA	AAGCTT	CTG	CTAGTCT			2021
ATGG	CAGCAT	CAAG	GCTGGT	ATTT	GCTACG	GCTG	ACCGCT	ACGC	CGCCG			2071
AATA	AGGGTA	CTGG	GCGGCC	CGTC	GAAAGGC	CCTT	TGGTTT	CAG	AAACCCA			2121
AGGCC	CCCCCT	CATA	CCAACG	TTTC	GACTTT	GATT	CTTGCC	GGT	ACGTGGT			2171
GGTGG	GTGCC	TTAG	CTCTT	CTCG	ATAGTT	AGAC						2205

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Fig. 2a

human homologue of mouse 4-1bb

h4-1bb Length 838

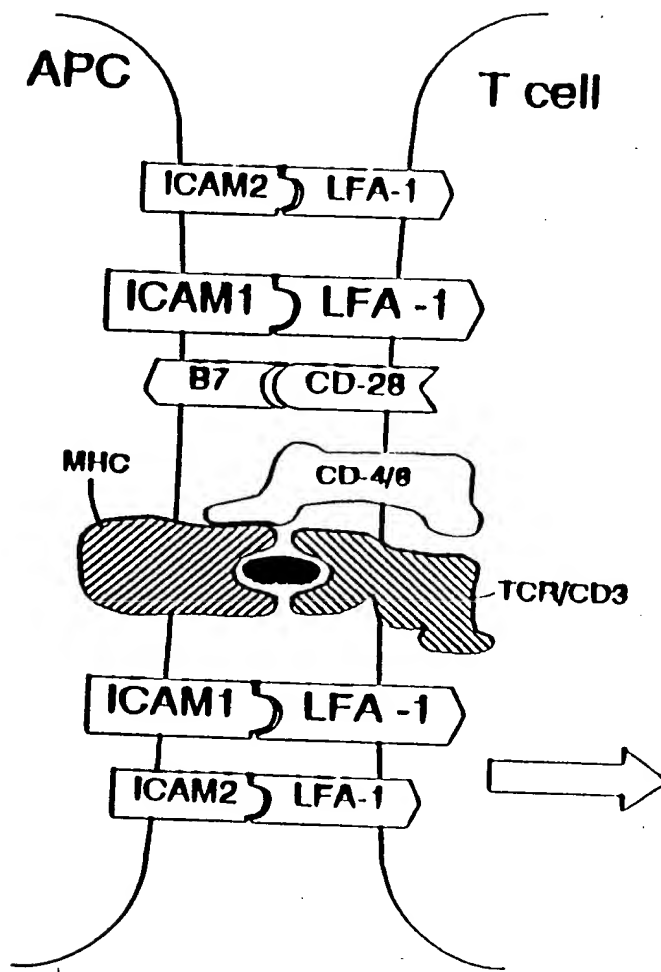
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101	ACAAGATCAT	TGCAGGATCC	TTGTAGTAAC	TGCCCAGCTG	GTACATTCTG
151	TGATAATAAC	AGGAATCAGA	TTTGCACTCC	CTGTCCTCCA	AATAGTTTCT
201	CCAGCGCAGG	TGGACAAAGG	ACCTGTGACA	TATGCAGGCA	GTGTAAGGT
251	GTTTTTCAGGA	CCAGGAAGGA	GTGTTCTTCC	ACCAGCAATG	CAGAGTGTGA
301	CTGCACTCCA	GGGTTTCACT	GCCTGGGGGC	AGGATGCAGC	ATGTGTGAAC
351	AGGATTGTAA	ACAAGGTCAA	GAAC TGACAA	AAAAAGGTTG	TAAAGACTGT
401	TGCTTTGGGA	CATTTAACGA	TCAGAAACGT	GGCATCTGTC	GACCTTGGAC
451	AAACTGTTCT	TTGGATGGAA	AGTCTGTGCT	TGTGAATGGG	ACGAAGGAGA
501	GGGACGTGGT	CTGTGGACCA	TCTCCAGCTG	ACCTCTCTCC	GGGAGCATCC
551	TCTGTGACCC	CGCCTGCCCC	TGCGAGAGAG	CCAGGACACT	CTCCGCAGAT
601	CATCTCCTTC	TTTCTTGCGC	TGACGTCGAC	TGCGTTGCTC	TTCTTGCTGT
651	TCTTCCTCAC	GCTCCGTTTC	TCTGTTGTTA	AACGGGGCAG	AAAGAACTC
701	CTGTATATAT	TCAAACAACC	ATTTATGAGA	CCAGTACAAA	CTACTCAAGA
751	GGAAGATGGC	TGTAGCTGCC	GATTTCCAGA	AGAAGAAGAA	GGAGGATGTG
801	AACTGTGAAA	TGGAAGTCAA	TAGGGCTGTT	GGGACTTT	

Fig. 2b

1	MGNSCYNIVA	TLLLVLNFER	TRSLQDFCSN	CPAGTFCDNN	RNQICSPCPP
51	NSFSSAGGQR	TCDICRQCKG	VERTRKECSS	TSNAECDCTP	GFHCLGAGCS
101	MCEQDCKQGQ	ELTKKGCKDC	CFGTFNDQKR	GICRPWTNCS	LDGKSVLVNG
151	TKERDVVCGP	SPADLSPGAS	SVTPFAPARE	FGHSPQIISF	FLALTSTALL
201	FLLFFLT LRF	SVVKRGRKKL	LYIFKQPFMR	PVQTTQEEDG	CSCRFPEEEE
251	GGCEL				

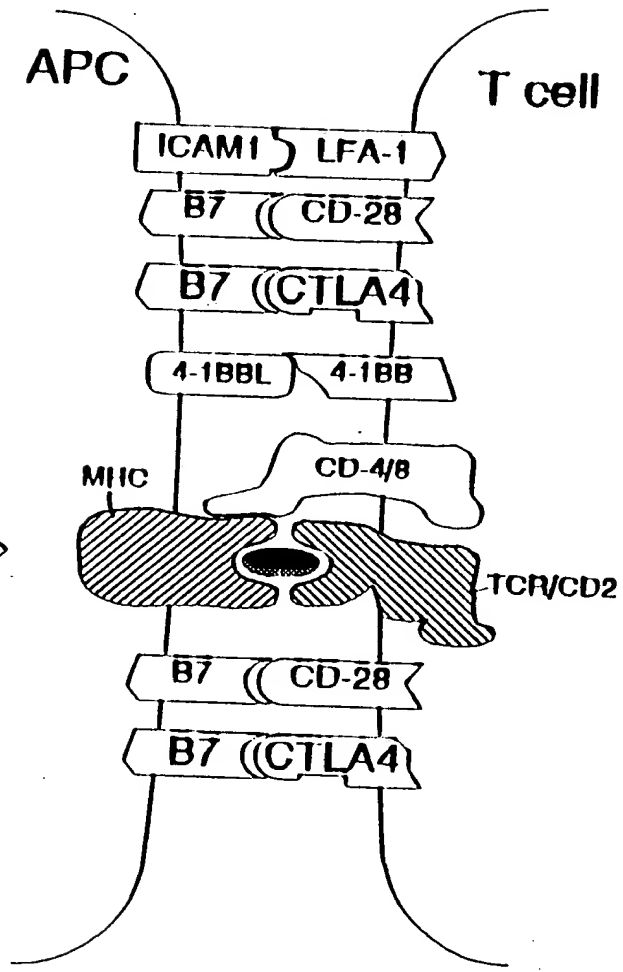
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COGNITIVE PHASE
early activation

Fig. 3a



PROLIFERATION
CLONAL EXPANSION
late activation

Fig. 3b

NORMAL T-CELL ACTIVATION PATHWAY

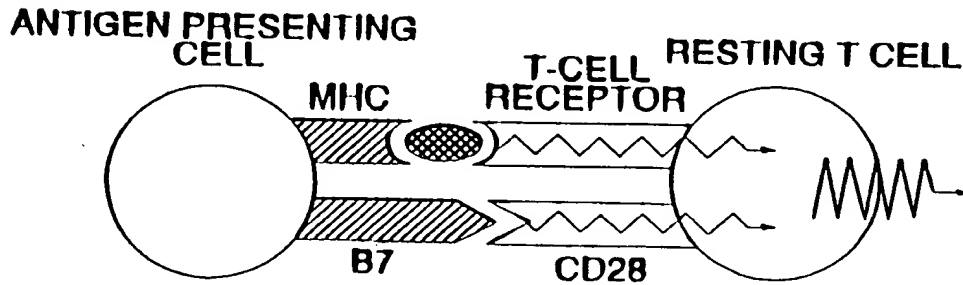


Fig. 4a

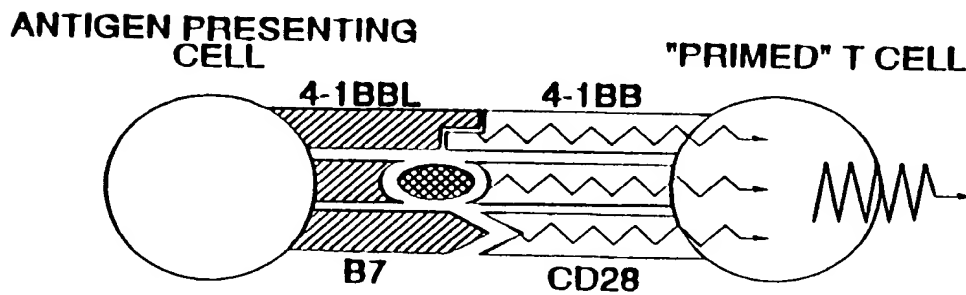


Fig. 4b

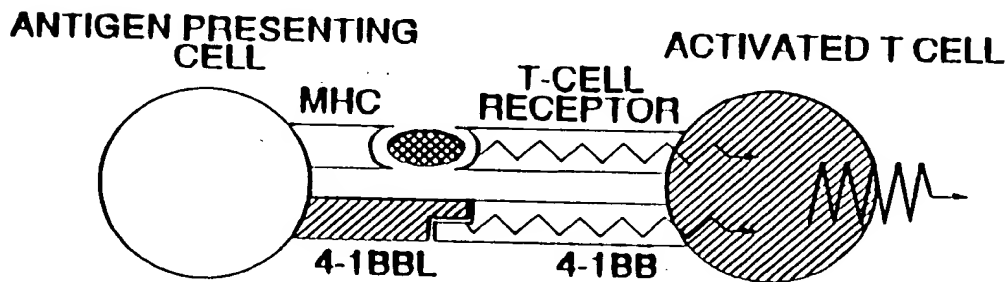


Fig. 4c

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BLOCKING STEPS IN T-CELL ACTIVATION PATHWAY

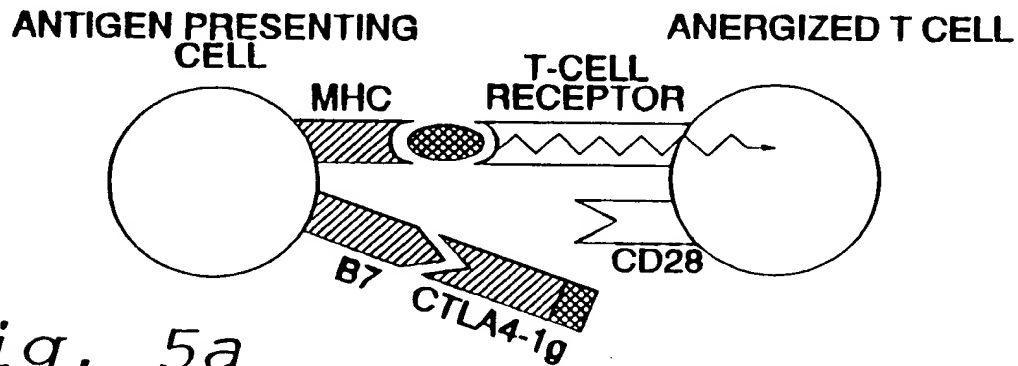


Fig. 5a

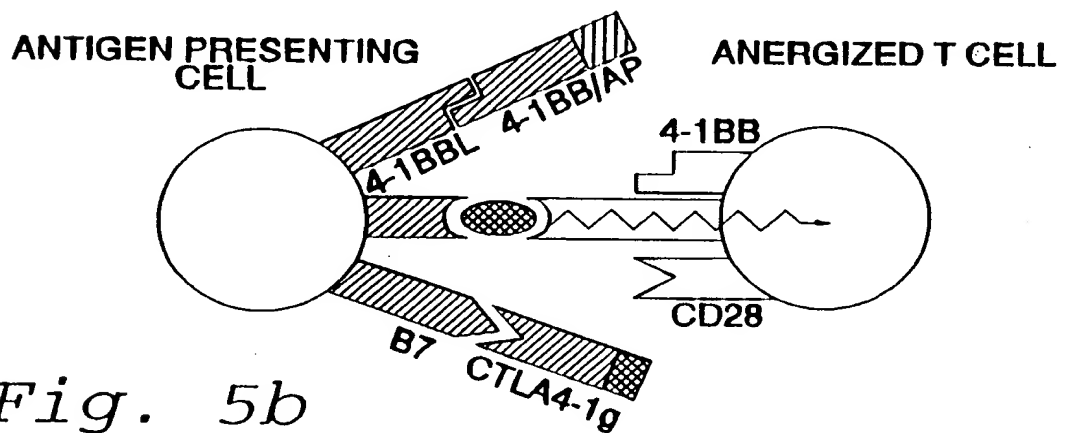


Fig. 5b

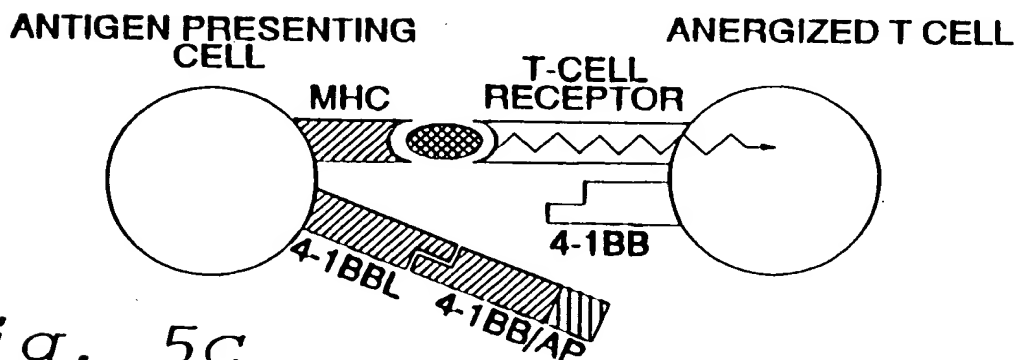


Fig. 5c